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Influence of Acute Aortic Insufficiency on the Hemodynamic Importance of a Coronary Artery Narrowing. II. Various Magnitudes of Aortic Insufficiency

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Coronary hemodynamic effects of controlled acute aortic insufficiency were studied in 40 open chest dogs with and without graded coronary diameter narrowing. An adjustable basket device was used to regulate aortic insufficiency, creating three groups: group 1, mild to moderate aortic insufficiency (regurgitant fraction < 50%); group 2, moderately severe aortic insufficiency (regurgitant fraction > 50%); and group 3, aortic insufficiency with mean aortic pressure restored to control levels. Mean coronary blood flow was similar to control values in group 1, but was higher in groups 2 and 3. The endocardial/epicardial flow ratio was similar with and without aortic insufficiency. With graded coronary narrowing greater than 80%, coronary flow and endocardial/epicardial flow ratio decreased with or without aortic insufficiency. However, endocardial/epicardial flow ratio usually decreased more during aortic insufficiency. Peak reactive hyperemic flow after release of a 10 second coronary occlusion also decreased during aortic insufficiency. The amount of decrease compared with control values was related to the magnitude of aortic insufficiency. This value with no coronary narrowing in group 1 was similar to peak reactive hyperemic flow with a 60% coronary narrowing during the control period. In group 2, peak reactive hyperemic flow was similar to that with an 80% coronary narrowing during the control period. Restoring mean aortic pressure to control values in group 3 did not restore peak reactive hyperemic flow to control values.

These data suggest that coronary flow reserve assessed with coronary narrowings or during reactive hyperemia is decreased during aortic insufficiency. The decrease in coronary flow reserve was more pronounced as the magnitude of aortic insufficiency increased.

Patients with aortic valve disease often have clinical findings that suggest myocardial ischemia (1). These findings usually imply valvular dysfunction of hemodynamic importance or accompanying coronary artery disease, or both. Using clinical findings alone, it is often difficult to distinguish ischemic manifestations related solely to valvular disease from those related to coexisting coronary artery disease. In patients without severe coronary artery disease, the mechanism by which either aortic stenosis or insufficiency produces transient myocardial ischemia is not clear. Changes in left ventricular mass and volume or changes in aortic and left ventricular pressures and aortic flow that accompany aortic valve disease might alter left ventricular perfusion at rest or during stress.

We have previously evaluated the influence of aortic stenosis on the hemodynamic importance of a coronary narrowing in an open chest dog model without left ventricular hypertrophy (2). We observed that changes in aortic and left ventricular pressures accompanying aortic stenosis seem sufficient to produce myocardial ischemia at rest and during stress. Preliminary studies in our laboratory also suggested similar findings during acute aortic insufficiency (3). This investigation expanded those observations and assessed the effects of both aortic insufficiency and coronary narrowing of different magnitudes on coronary blood flow.

Methods

Animal preparations. Forty large healthy dogs (weight range 20 to 40 kg) were studied. Data from 10 of these dogs have been reported (3). After premedication (morphine, 1

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mg/kg), dogs were anesthetized (alpha-chloralose, 100 mg/kg or pentobarbitol, 30 mg/kg) and intubated. Respiration was controlled using a Bird Mark 7 respirator and a fraction of inspired oxygen (FIO_2) of 40% to maintain arterial blood gases and pH within the physiologic range. A left thoracotomy was performed in the fifth intercostal space and the heart was supported by a pericardial cradle. Both carotid arteries, the ascending aorta and either the left circumflex or anterior descending coronary artery were isolated.

Instrumentation. Electromagnetic flow probes (Biotronex) were positioned on the proximal coronary artery and ascending aorta. Use and calibration of these probes in our laboratory have been described previously (3–5). The flowmeter was operated at a frequency that provided a constant amplitude within ± 5% from 0 to 47 Hz and a linear phase shift. Calibration and linearity of the flow probes were obtained by means of a hydraulic system similar to that used by Malooly et al. (6). Physiologic saline solution was pumped in both directions over several flow rates through a section of artery containing the flow probe. The flowmeter output was linear (bidirectional) over the range of flows recorded in this study. Catheter tip micromanometers (Millar) were positioned in the left ventricle from the right carotid artery and left atrial appendage. After confirmation of equally sensitive calibration, the catheter positioned from the right carotid artery was withdrawn to the ascending aorta.

Creation of coronary narrowings. Two techniques were used to create controlled reduction of coronary diameter. A calibrated snare was used in 12 dogs. In the other 28 dogs, narrowings were created with 1 mm long plastic occluders, chosen to produce estimated reductions in diameter of 60, 80 and 90%. These narrowings were chosen because previous experiments (2–5) showed that 1 mm long narrowings of increasing diameter reduction produced a sequence of increasing alterations on coronary hemodynamics.

Creation of reversible aortic insufficiency. In 12 experiments, reversible aortic insufficiency was created with a modified collapsible metal basket catheter (Dotter Retriever, Cook Catheter Company). Because the metal basket often created unacceptable noise in the aortic flow signal, we made a collapsible plastic basket that did not alter the magnetic field of the aortic flow probe and used it in 28 experiments. It is positioned in the left ventricle through a stab wound at the apex or from a carotid artery. Manipulation of the basket catheter at the level of the aortic valve allowed creation of various magnitudes of aortic insufficiency. In six experiments during aortic insufficiency, mean aortic pressure was restored to values obtained during the control period by partial occlusion of the descending thoracic aorta.

Measurement of endocardial/epicardial flow ratio. This ratio was determined with and without aortic insufficiency by the radioactive microsphere (8 to 10 μm) technique in 24 experiments (7). Injections of more than 3 million spheres were made into the left atrium. These injections were performed when a 90% coronary narrowing was applied. Thus, either the anterior or posterior left ventricular region was perfused by an artery with 90% narrowing while the other left ventricular region was perfused by an artery without narrowing.

At the conclusion of the experiment, the dogs were given a lethal dose of potassium chloride. The heart was removed and fixed in formalin solution for 72 hours. The left ventricle was "sectioned" into four slices along its long axis. Samples from the anterior and posterior papillary muscle regions of the middle two slices were divided into endocardial, midwall and epicardial pieces and weighed. The number of radioactive counts per gram in the endocardial and epicardial pieces was used to calculate endocardial/epicardial flow ratios. Two values in each dog were obtained by averaging ratios from all anterior and posterior region samples. Values were grouped according to whether perfusion was through a coronary artery with or without narrowing.

Measurement of endocardial segment length and function. Endocardial left ventricular dimension and motion were assessed in the anterior region during eight experiments using miniature (0.5 × 2 × 2 mm) ultrasonic crystals energized by a Norland 202 sonomicrometer (8). In these experiments, graded diameter reductions were created on the anterior descending artery above the region where the crystals were placed. In each experiment, total anterior descending artery occlusion caused a rapid and major effect on systolic shortening. Maximal distance separating the endocardial crystals during the control period in diastole without coronary narrowing was estimated by measuring crystal separation in the potassium-arrested heart at the end of the experiment. From calibrated ultrasonic crystal signals, change from control period crystal separation was measured. Maximal and minimal diameter and segment shortening fraction were calculated at each degree of coronary narrowing. In all experiments in which the endocardial/epicardial flow ratio and endocardial motion were measured, coronary narrowings were created with plastic occluders.

Typical experiment. Each experiment consisted of three periods beginning with a *first control period*. Each period consisted of a "sequence" of duplicate recordings at fast (100 mm/s) and slow (2.5 mm/s) rates of coronary and aortic flow, as well as aortic and left ventricular pressure signals before and after a 10 second complete coronary occlusion. This sequence was repeated after a 60% and an 80% coronary narrowing had been applied for 5 minutes. The 10 second coronary occlusion was omitted after a 90% coronary narrowing was applied. During the *period of aortic insufficiency*, the basket was opened and positioned across the aortic valve while flow and pressure signals were monitored. When aortic insufficiency was obtained, as indicated by a marked increase in the negative component of the diastolic aortic flow signal, the position of the basket was fixed. Flow

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and pressure stabilization (± 5%) occurred in less than 5 minutes, and a total of approximately 10 minutes was allowed before measurements were made. During a *second control period*, the basket was repositioned so that no aortic insufficiency was present. Five minutes after pressure and flows stabilized, recordings were repeated according to sequences outlined for the first control period.

If differences between duplicate responses within a period were more than 10%, the sequence was not used in this study. When differences of 10% or less were found between paired reactive hyperemic responses, the higher value was used. However, if small differences (≤ 10%) were found by comparing systemic or coronary hemodynamic values or left ventricular dimensions from the two control periods, the value closest to that obtained during aortic insufficiency was compared with values during aortic insufficiency.

Measurements and calculations. Total coronary blood flow before a 10 second occlusion was used as an index of basal flow. Peak reactive hyperemic flow was used as an index of flow reserve. Coronary artery resistance was calculated as the ratio of mean aortic pressure and mean coronary flow. The portion of the aortic signal in the latter third of diastole, before creation of aortic insufficiency, was taken as zero aortic flow baseline (6). After creation of aortic insufficiency, total forward stroke volume was taken as the area under the flow tracing above the zero baseline. Regurgitant stroke volume was taken as the area below the zero baseline (3,6,9). Regurgitant fraction was obtained as the ratio of regurgitant and total forward stroke volume (3,6,9). Systolic and diastolic phasic coronary flows and aortic flow were quantified by cutting out these areas and weighing them on an analytic balance. We have found that this technique yields a coefficient of variation less than 1%. All measurements were made over at least 10 heartbeats and averaged during control and aortic insufficiency periods with no coronary diameter reduction and with narrowings estimated at 60, 80 and 90%.

Confirmation studies. The position and depth of ultrasonic crystals were measured. The area immediately surrounding both crystal pairs was not used in subsequent radioactive counts. Aortic valve leaflets were examined for possible damage, and the aortic root was filled with saline solution to confirm aortic valve competence. To evaluate the degree of diameter reduction created during experiments by an independent technique, we again placed the plastic occluders on the isolated coronary artery in seven dogs. Polysulfide was injected into the left main coronary artery. After hardening, the cast of the artery and its narrowed regions was dissected free. The actual coronary artery and narrowing diameters were measured with calipers.

Analysis of results. Mean values and standard deviations were calculated. An analysis of variance for repeated measures, Duncan's multiple comparison procedure and a paired *t* test were used for statistical comparisons. A probability [p] value less than 0.05 was considered statistically significant. Experiments were separated into three groups depending on the magnitude of aortic insufficiency: group 1, mild to moderate aortic insufficiency (regurgitant fraction < 50%); group 2, moderately severe aortic insufficiency (regurgitant fraction > 50%); and group 3, aortic insufficiency with mean aortic pressure restored to control levels.

Results

All dogs had competent aortic valves. Casts showed that plastic occluders estimated to produce a 60% coronary diameter narrowing actually produced a narrowing that averaged 56 ± 9% (range 41 to 69). Occluders estimated on an 80% narrowing produced narrowings of 72 ± 5% (range 65 to 78) and those estimated at 90% produced narrowings of 82 ± 2% (range 80 to 84). For simplicity we used the estimated values throughout the Results and Discussion sections.

Aortic and ventricular hemodynamic responses (Table 1). During aortic insufficiency, regurgitant fractions averaged 31% in group 1 (mild to moderate insufficiency), 66% in group 2 (moderately severe insufficiency) and 38% in group 3 (insufficiency with aortic pressure returned to normal). Heart rate was similar during aortic insufficiency and during the control period. Aortic systolic pressure was similar during the control period and in groups 1 and 2, but was higher in group 3 ($p < 0.05$). Aortic diastolic pressure decreased with increasing magnitudes of aortic insufficiency (all groups $p < 0.05$ compared with control period values). Aortic diastolic pressure was lower in group 2 than in groups 1 and 3 ($p < 0.05$). Left ventricular end-diastolic pressure was consistently higher during aortic insufficiency, but similar when the three groups with aortic insufficienty were compared.

Coronary hemodynamic responses (Tables 2 and 3). Mean coronary blood flow with no coronary narrowing was similar during the control period and in group 1. However, mean coronary flow increased modestly in groups 2 and 3 (17 and 23%, respectively; both $p < 0.05$). The portion of coronary blood flow occurring during diastole decreased during aortic insufficiency of all magnitudes (all $p < 0.05$). This value was lower in group 2 (moderately severe insufficiency) than in group 1 (mild and moderate insufficiency) ($p < 0.05$). A reversal of diastolic coronary flow during end-diastole was often observed in group 2. In the 24 experiments in which the endocardial/epicardial flow ratio was measured, it was not consistently changed regardless of the magnitude of aortic insufficiency. As the degree of coronary narrowing increased, mean coronary flow in groups 2 and 3 initially remained higher than control values, but this was no longer true with a coronary narrowing of sufficient severity to decrease mean coronary flow.

Table 1. Summary of Aortic and Left Ventricular Hemodynamic Findings in Acute Aortic Insufficiency

	HR (beats/min)		Pressures (mm Hg)							
			Mean Ao		AoS		AoD		LVED	
Exp. No.	C	AI	C	AI	C	AI	C	AI	C	AI
Group 1. Aortic Insufficiency (mild to moderate)										
1	130	130	125	118	147	150	114	102	6	15
2	130	135	120	110	144	138	108	96	6	15
3	180	180	98	103	113	122	90	93	12	24
4	180	180	113	97	131	131	104	80	21	24
5	100	105	139	132	174	183	122	107	12	15
6	130	130	109	117	134	154	96	99	10	22
7	130	130	127	123	150	150	115	109	3	13
8	130	120	88	68	108	99	76	52	4	5
9	130	130	99	103	122	127	88	90	4	7
10	110	103	96	88	118	118	85	73	5	5
11	150	155	122	108	143	139	112	92	10	17
12	130	140	107	109	130	142	95	92	7	18
13	107	97	119	100	140	140	108	80	5	10
14	143	145	112	93	137	130	100	74	11	15
15	150	160	145	107	170	136	133	92	10	14
16	142	140	104	77	112	106	100	63	3	10
17	160	136	145	114	157	128	139	107	9	10
18	113	125	120	88	131	119	116	73	4	6
19	123	120	96	87	128	125	80	68	3	9
20	111	107	99	65	122	106	88	45	3	10
21	156	188	103	82	124	105	93	71	3	6
22	150	143	90	69	99	86	86	40	7	10
Mean	136	136	113	98	133	129	102	82	7	13
± SD	22	25	17	19	19	21	17	20	4	6
Group 2. Aortic Insufficiency (moderately severe)										
23	140	100	108	70	130	131	97	40	5	16
24	120	120	103	82	130	120	90	63	5	8
25	136	136	96	78	126	120	81	57	6	12
26	120	120	175	155	195	180	50	115	10	15
27	135	130	108	67	133	107	95	47	6	13
28	130	130	80	69	100	100	70	53	7	10
29	140	150	107	79	130	134	95	51	7	13
30	125	120	96	75	113	113	88	56	6	13
31	95	95	118	83	129	122	112	63	8	17
32	125	130	69	51	86	78	60	39	3	5
33	143	143	97	66	106	102	93	48	6	8
34	150	143	162	106	191	137	148	90	8	11
Mean	130	126	110	82	131	120	90	60	6	12
± SD	15	17	30	27	33	25	25	22	2	4
Group 3. Aortic Insufficiency (restored mean aortic pressure)										
35	150	150	99	100	119	162	86	76	3	10
36	175	175	132	136	155	208	116	100	10	13
37	140	140	113	112	135	188	102	76	3	10
38	205	214	100	91	116	116	92	79	0	0
39	128	133	84	88	101	143	75	47	10	10
40	158	166	106	94	125	159	97	62	5	10
Mean	159	163	106	104	125	163	95	73	5	9
± SD	28	30	16	18	18	33	14	18	4	5

AI = aortic insufficiency; AoD = diastolic aortic pressure; AoS = systolic aortic pressure, C = control; Exp. No. = experiment number, HR = heart rate, LVED = left ventricular end-diastolic pressure; mean Ao = mean aortic pressure; SD = standard deviation

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Table 2. Summary of Coronary Hemodynamic Findings in Acute Aortic Insufficiency

Exp. No.	CBF (ml/min) No CN		Diastolic CBF %		CBF (ml/min) 90% CN		Peak Reactive Hyperemic CBF (ml/min) No CN		60% CN		80% CN		Regurgitant Fraction
	C	AI	C	AI	C	AI	C	AI	C	AI	C	AI	
Group 1. Aortic Insufficiency (mild to moderate)													
1	64	57	81	67	53	49	275	177	230	165	105	91	40
2	70	82	86	67	57	49	308	246	280	213	140	115	40
3	39	39	75	60	22	31	117	86	101	86	94	68	25
4	39	34	75	62	31	28	117	75	101	75	94	60	40
5	47	47	93	87	27	31	165	118	132	108	108	75	40
6	57	76	83	70	52	46	165	144	148	137	108	91	38
7	48	54	78	73	42	44	144	124	120	113	96	70	35
8	22	24	78	71	18	18	73	62	62	58	38	31	33
9	24	24	87	75	15	18	115	94	86	72	67	48	33
10	34	52	86	77	30	30	129	125	119	10	69	65	30
11	14	18	82	72	11	11	63	77	56	65	34	36	20
12	24	27	77	70	15	18	70	61	60	52	46	40	25
13	40	45	81	69	30	30	135	135	110	125	75	70	30
14	60	60	70	73	34	17	136	94	111	60	102	60	33
15	51	32	86	62	32	19	179	102	140	77	ND	ND	20
16	53	62	74	63	35	35	220	174	174	141	141	132	25
17	42	51	76	69	36	42	105	54	75	57	54	33	40
18	43	35	86	77	—	—	73	73	69	59	—	—	13
19	40	43	80	75	33	33	95	83	78	83	71	56	21
20	43	40	81	67	21	17	139	102	—	—	—	—	10
21	30	24	81	70	18	4	78	36	58	30	44	24	48
22	34	26	88	57	22	17	108	73	82	69	52	65	38
Mean	41.9	43.7	77.6	69.7	30 7	26.0	136.5	105.4	113.9	88.3	81.0	64.7	30.8
± SD	14.3	16.9	16.4	6.7	13.1	13.3	63.1	48 3	57.4	47.4	32 3	28.1	9 9
Group 2. Aortic Insufficiency (moderately severe)													
23	18	19	86	50	13	18	90	53	68	51	56	38	60
24	43	43	86	58	30	30	172	108	151	82	108	43	60
25	40	48	72	61	24	24	108	80	96	72	56	48	62
26	45	58	81	60	32	45	185	166	153	133	104	87	67
27	28	30	77	05	20	20	120	39	95	34	73	30	80
28	24	40	80	60	20	20	89	64	82	56	43	40	70
29	27	34	77	56	14	17	76	51	65	48	50	36	71
30	69	81	87	64	46	35	276	230	173	161	127	92	67
31	35	39	84	44	ND	ND	105	39	ND	ND	ND	ND	65
32	19	26	79	50	4	4	45	34	45	9	28	15	68
33	30	35	86	68	20	25	95	75	95	65	65	53	73
34	46	41	81	79	—	—	143	78	78	46	64	41	52
Mean	35.3	41.2	81.3	54.6	22.3	23.8	125.3	84.8	100.1	68.8	70.4	47.6	66.3
± SD	14.4	16 1	4.6	18.1	11.7	11.1	61 7	58 6	41.1	43.6	30.3	23.0	7.2
Group 3. Aortic Pressure (restored mean aortic pressure)													
35	79	126	86	52	40	40	316	300	292	237	174	142	35
36	60	75	91	76	45	70	300	300	210	240	175	180	33
37	65	52	86	59	27	39	130	104	104	91	91	65	37
38	57	66	88	77	43	50	163	123	128	88	101	79	25
39	53	62	89	46	33	33	188	160	111	94	86	57	50
40	70	90	82	57	41	35	116	128	150	87	116	70	50
Mean	64.0	78.5	87.0	61.2	38.2	42 8	213.8	185.8	165.8	139.5	123.8	98.8	38.3
± SD	9.5	26.6	3.1	12.7	6.8	10.3	76.0	90.2	72.6	76.7	40.6	50.1	9.9

AI = aortic insufficiency, C = control, CBF = coronary blood flow, CN = coronary narrowing, Exp No = experiment number, SD = standard deviation; ND = not determined

Table 3. Summary of Transmural Flow Distribution in Acute Aortic Insufficiency*

	Endocardial/Epicardial Flow Ratio			
	No Coronary Narrowing		90% Coronary Narrowing	
	C	AI	C	AI
Group 1 and 2. Aortic Insufficiency (mild to moderate and moderately severe)				
	1.02	1.14	—	—
	0.95	0.97	1.23	1.17
	1 42	0.88	0.77	0.06
	1 14	0.58	0.58	0.18
	1.10	1.11	0.92	1.13
	1.32	1.03	—	—
	1.43	0.72	—	—
	1.08	1.08	—	—
	0.78	0.83	0.90	1.00
	0.85	1.25	—	—
	1.23	1.11	1.11	0
	1.43	0.72	—	—
	1.39	0.74	1.18	0.94
	0.85	0.92	0.99	0.97
	0.85	1.06	0.99	0 95
	1 24	1.14	0.87	0.51
	1.23	1.40	1.13	0.71
	1.23	1.30	1.10	1.10
Mean	1.14	1.00	0.98	0.73
± SD	0.22	0.22	0.19	0.43
Group 3. Aortic Insufficiency (restored aortic pressure)				
	1.24	0.94	1.19	0.88
	1.01	1.18	0.70	0.88
	1.15	0.88	0.56	0.43
	1.19	1.09	1.04	0.87
	0.99	1.05	0.88	0 95
	1.40	0.45	0.94	0.12
Mean	1.16	0.93	0 90	0.69
± SD	0.15	0.26	0.23	0.34

*Studies were performed in a small subgroup of the experiments and individual experiments are not listed
AI = aortic insufficiency, C = control, SD = standard deviation

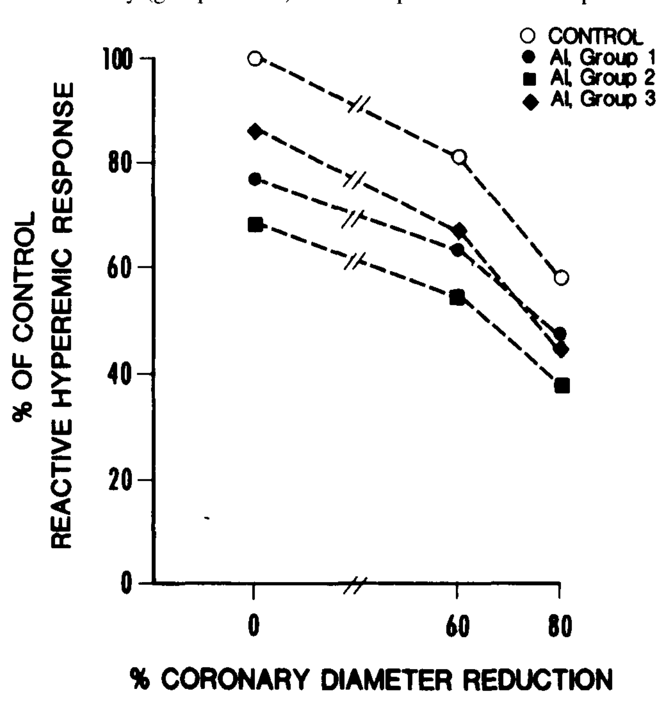
mean coronary flow decreased, the endocardial/epicardial flow ratio also decreased with or without aortic insufficiency (both $p < 0.05$). However, this decrease in flow ratio was usually more pronounced during aortic insufficiency ($p < 0.05$).

Mean coronary resistance was modestly decreased in group 1 (3.11 ± 1.50 to 2.60 ± 1.12 mm Hg/ml per min, $p < 0.05$) and decreased by a larger amount in group 2 (3.41 ± 1.11 to 2.14 ± 0.68 mm Hg/ml per min, $p < 0.05$). Mean coronary resistance was also decreased in group 3 (1.70 ± 0.31 to 1.44 ± 0.50 mm Hg/ml per min, $p < 0.05$).

Peak reactive hyperemic flow with no coronary narrowing was consistently reduced during aortic insufficiency as compared with control values (23% in group 1, 32% in group 2 and 13% in group 3; all $p < 0.05$) (Fig. 1 and 2). The reactive hyperemic response was reduced more in group 2 than in group 1 ($p < 0.05$). Restoring mean aortic pressure to control values in group 3 returned the reactive hyperemic response toward, but not to, values obtained during the control period. Application of 60% and 80% coronary narrowings reduced peak hyperemic responses with and without aortic insufficiency. However, peak reactive hyperemic flow was consistently less during aortic insufficiency and coronary narrowing than it was during the control period with the same coronary narrowing (all $p < 0.05$). Again, reactive hyperemic flow was reduced more in group 2 than in group 1 ($p < 0.05$). Restoring mean aortic pressure to control values in group 3 only partially restored the reactive hyperemic response.

Regional left ventricular endocardial dimension and function. Depth of the crystals was 10 ± 2 mm (range 9 to 14). Left ventricular end-diastolic diameter consistently increased during aortic insufficiency (15.4 ± 2.7 to 16.6 ± 3.7 mm, $p < 0.05$), but end-systolic diameter was not significantly changed (12.6 ± 1.8 to 12.7 ± 1.8 mm, $p < 0.05$). The percent fractional shortening increased slightly during aortic insufficiency without coronary narrowing (16 ± 11 to 22 ± 10%, $p < 0.05$). With application of graded coronary narrowing, no significant change in dimensions occurred with or without aortic insufficiency with narrowings less than 90%. With a 90% narrowing, both end-dia-

Figure 1. Summary of effect of aortic insufficiency (AI) on coronary flow reserve. The reactive hyperemic response during the control period and with no coronary narrowing was considered 100%. Responses with a coronary narrowing and during aortic insufficiency (groups 1 to 3) were compared with this response.



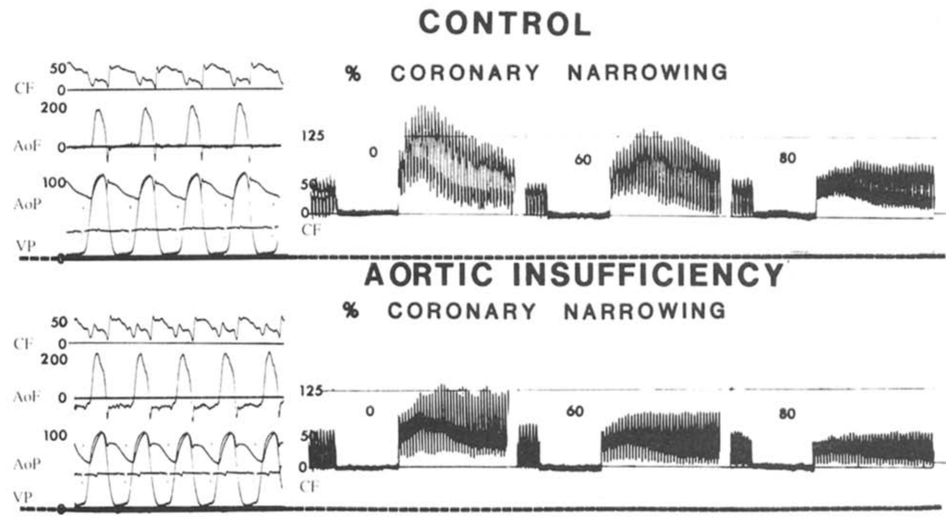


Figure 2. Representative example of coronary (ml/min) and aortic (ml/s) flows and aortic and left ventricular pressures (mm Hg) during the control and aortic insufficiency periods. During aortic insufficiency, the portion of coronary flow during systole increased as aortic diastolic pressure decreased and left ventricular diastolic pressure increased. Also during aortic insufficiency, reactive hyperemic flow with and without coronary narrowing decreased. AoF = aortic flow; AoP = aortic pressure; CF = coronary flow; VP = ventricular pressure.

stolic (15.9 ± 3.1 and 17.4 ± 3.9 mm) and end-systolic (13.4 ± 2.2 and 13.9 ± 2.8 mm) dimensions were usually larger with or without aortic insufficiency than when no coronary narrowing was applied (all $p < 0.05$). End-diastolic diameters were larger during aortic insufficiency than during the control period ($p < 0.05$), but end-systolic diameters were not. Percent fractional shortening decreased with the 90% coronary narrowing with or without aortic insufficiency (15 ± 9 and 20 ± 8%, $p < 0.05$) and continued to be slightly greater during aortic insufficiency ($p < 0.05$).

Discussion

Coronary flow reserve during aortic insufficiency. These experiments suggest that coronary flow reserve was limited during acute aortic insufficiency and that this limitation was more marked as the magnitude of aortic insufficiency increased. Evidence for decreased coronary flow reserve was demonstrated in several ways. First, peak reactive hyperemic flow responses were decreased during aortic insufficiency, and as the magnitude of aortic insufficiency increased, the reduction in peak reactive hyperemic flow also increased. Additionally, when a coronary artery narrowing was present during aortic insufficiency, an important reduction in peak reactive hyperemic flow occurred compared with control values having comparable degrees of coronary narrowing. Second, with 90% coronary narrowing, which decreased coronary flow at rest, the decrease in coronary flow (that is, coronary flow with no narrowing minus coronary flow with 90% narrowing) was greater when aortic insufficiency was present. This deleterious effect of aortic insufficiency occurred with all magnitudes of aortic insufficiency, but was more prominent as the magnitude of aortic insufficiency increased. Third, the endocardial/epicardial flow ratio was preserved during aortic insufficiency and no coronary narrowing. When a 90% coronary narrowing was applied, the endocardial/epicardial flow ratio decreased with or without aortic insufficiency. However, during aortic insufficiency, the decrease in the flow ratio was greater than during the control period. These findings confirm our previous observations that coronary flow reserve was decreased during aortic insufficiency. Both coronary narrowings and increasing magnitudes of aortic insufficiency potentiated the reduction in coronary flow reserve observed during mild aortic insufficiency.

Mechanisms of reduced coronary flow reserve. The mechanisms responsible for the reduction in coronary flow reserve during aortic insufficiency can only be partially determined from this study. Declining aortic diastolic and mean pressures during aortic insufficiency certainly contribute to the reduced coronary flow reserve. When mean aortic pressure was restored to control values, diastolic aortic pressure increased but remained below control values; this only partially restored reactive hyperemic flow (Fig. 1). Other contributing mechanisms remain speculative. During aortic insufficiency, retrograde aortic flow occurs in diastole. Reversal of aortic flow may also reverse diatolic coronary flow; this reversal has been reported for severe aortic insufficiency (3,9–12).

Left ventricular function. Regional left ventricular endocardial dimensions were measured in only a few studies. As expected, left ventricular dilation occurred during acute aortic insufficiency. Regional left ventricular function as estimated by percent fractional shortening appeared preserved during aortic insufficiency. Additionally, with application of a 90% coronary narrowing, left ventricular dimension increased with or without aortic insufficiency; percent fractional shortening also remained slightly greater during aortic insufficiency than during the control period. Therefore, if the lower endocardial/epicardial flow ratio during aortic insufficiency and a 90% coronary narrowing can be interpreted as indicative of potential myocardial ischemia, the magnitude of ischemia must have been mild because the regional shortening fraction remained greater than control values. Perhaps this was compensated by means of a Frank-Starling mechanism.

The increases in left ventricular end-diastolic dimension (average 8%) and end-diastolic pressure (4 to 6 mm Hg) during acute aortic insufficiency were only modest, but changes in end-diastolic pressure were consistent with reports of other investigators (11,13). Additionally, the similarity in left ventricular end-diastolic pressure during acute aortic insufficiency in the group with mild to moderate aortic insufficiency (group 1) and the group with more severe aortic insufficiency (group 2) was surprising. Both Falsetti et al. (11) and Griggs and Chen (13) also reported similar left ventricular end-diastolic pressures when comparing groups with various magnitudes of acute aortic insufficiency. Rembert et al. (12) produced acute aortic insufficiency more severe than that produced in other studies and reported larger increases left ventricular end-diastolic pressure.

Coronary blood flow. The coronary hemodynamic findings obtained in a large number of animals with various magnitudes of aortic insufficiency are helpful in understanding some previously reported conflicting results about the effect of acute aortic insufficiency on coronary flow. Previous studies (9–18) reported an increase, no change or a decrease in mean coronary flow during acute aortic insufficiency. Our study demonstrates that mean coronary flow usually increases only during moderately severe aortic insufficiency or when mean aortic pressure is restored to control values during aortic insufficiency of lesser magnitudes. When the coronary artery is not narrowed during mild to moderate and more severe aortic insufficiency, the finding that the endocardial/epicardial flow ratio was similar to control values agrees with previous findings of other investigators (11). However, in models of acute aortic insufficiency, severe enough to produce acute left ventricular failure (12) or an aortic diastolic pressure below 40 mm Hg (13), endocardial perfusion appears compromised.

Comparison with aortic stenosis. It is interesting to compare these data with other data we have obtained in acute aortic stenosis created at a subcoronary level (2) because different coronary hemodynamic changes were seen during acute aortic insufficiency and aortic stenosis. Aortic stenosis more consistently increased mean coronary flow and decreased the endocardial/epicardial flow ratio. The coronary flow occurring during diastole decreased during aortic stenosis and increased during aortic insufficiency. Reactive hyperemic responses decreased during both aortic insufficiency and aortic stenosis. With the application of a 90% coronary narrowing, mean coronary flow decreased proportionately more during both aortic insufficiency and aortic stenosis than during the control period. Concomitantly, the endocardial/epicardial flow ratio decreased during either aortic insufficiency or aortic stenosis and decreased more than during the control period. These changes were obtained in models without left ventricular hypertrophy, which itself could produce decreases in coronary reserve.

In summary, at rest the endocardial/epicardial flow ratio is more likely to be normal during aortic insufficiency but abnormal during aortic stenosis. During the stress produced by either coronary narrowing or exercise, or both, coronary reserve would be expected to be decreased during both aortic insufficiency and aortic stenosis. Coronary hemodynamic alterations were usually more marked during aortic stenosis than during aortic insufficiency. This finding correlates with the clinical observation that evidence for myocardial ischemia is more common in patients with aortic stenosis than in those with aortic insufficiency.

Potential limitations of study. Several limitations of this study deserve comment. First, as expected, aortic insufficiency changed mean and diastolic aortic and end-diastolic left ventricular pressures. Results in the dogs in which mean aortic pressure was restored to control values during aortic insufficiency (group 3) suggested that altered coronary hemodynamics were not due solely to changes in mean aortic pressure. However, the lower aortic diastolic and higher left ventricular end-diastolic pressures during aortic insufficiency certainly contributed to the alterations in coronary hemodynamics in this acute animal model and would contribute also to any changes in coronary hemodynamics that occur in patients (19). Second, all dogs studied had sinus tachycardia. The full hemodynamic effect of aortic insufficiency on the coronary circulation and left ventricular function could have been altered by tachycardia. Tachycardia would diminish the magnitude of aortic insufficiency, but increased metabolic demands related to the tachycardia would have a deleterious effect. Third, both aortic insufficiency and coronary narrowings were maintained for a relatively short period of time, and any possible compensatory left ventricular or coronary hemodynamic alterations over time were not addressed. Fourth, left ventricular dilation and hypertrophy which occur in chronic aortic insufficiency may produce effects on coronary hemodynamics independent of or in addition to coronary hemodynamic changes that occur because of acute changes in aortic flow and aortic and left ventricular pressures induced in this model (20–23). Finally, these studies were performed in acute open chest dogs; coronary hemodynamic responses in patients with either acute or chronic aortic insufficiency may differ.

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